

What is claimed is:

1. A non-human transgenic animal whose genome comprises a first nucleotide sequence encoding human CD20 and a second nucleotide sequence encoding a subunit of a heterologous FcγIII receptor.
2. The transgenic animal of claim 1 wherein said first nucleotide sequence is operably linked to a human endogenous promoter.
3. The transgenic animal of claim 2 whose cells express human CD20.
4. The transgenic animal of claim 3 wherein human CD20 is expressed on the surface of B lymphocytes.
5. The transgenic animal of claim 2, wherein said second nucleotide sequence is operably linked to a human endogenous promoter.
6. The transgenic animal of claim 1 wherein said second nucleotide sequence encodes human CD16 alpha chain subtype A.
7. The transgenic animal of claim 6 wherein said receptor is expressed on the surface of leucocytes.
8. The transgenic animal of claim 7 wherein said receptor is expressed on the surface of a cell comprising NK cells, macrophages, neutrophils, eosinophils, basophils, mast cells or thymocyte cells or mixtures thereof.
9. The transgenic animal of claim 1 wherein the genome of said animal further comprises a disruption in an endogenous gene encoding a subunit of a receptor substantially homologous to the heterologous FcγIII receptor.
10. The transgenic animal of claim 9, wherein the endogenous gene encodes a murine CD16 alpha chain.

11. A method of identifying an agent capable of treating a B cell lymphoma said method comprising:
- a) measuring the level of B lymphocytes expressing human CD20 in an animal of claims 1 or 9;
  - b) administering said agent to the animal of claims 1 or 9; and
  - c) measuring the level of B lymphocytes expressing human CD20 in the animal;
- wherein a decrease in the number of B lymphocytes expressing human CD20 in the animal after treatment with the agent identifies the agent capable of treating a B cell lymphoma.
12. An agent identified according to claim 11.
13. A method of identifying an agent capable of depleting or killing cells expressing human CD20 said method comprising:
- a) measuring the level of B lymphocytes expressing human CD20 in an animal of claims 1 or 9;
  - b) administering said agent to the animal of claims 1 or 9; and
  - c) measuring the level of B lymphocytes expressing human CD20 in the animal;
- wherein a decrease in the number of B lymphocytes expressing human CD20 in the animal identifies the agent as capable of depleting or killing cells expressing CD20.
14. The method of claim 13 wherein said cells are cancer cells.
15. An agent identified according to claim 14.
16. A cell or tissue derived from the transgenic animal of claim 1 or 9.
17. The transgenic animal of claim 1 or 9 wherein said animal is a rodent.
18. The transgenic animal of claim 17 wherein said rodent is a mouse.

19. A method of identifying an agent capable of inducing an Fc-mediated effector cell response said method comprising

- a) measuring the baseline level of one or more cytokines associated with an Fc-mediated effector cell response in a transgenic animal of claim 1;
- b) administering said agent to the transgenic animal;
- c) measuring the level of the cytokines in the animal;  
wherein an increase in the level of cytokines after administration identifies the agent as capable of inducing an Fc-mediated effector cell response.

20. A method of identifying an agent capable of inducing an Fc-mediated effector cell response against B lymphocytes expressing human CD20, said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in a first transgenic animal ;
- b) administering said agent to the first transgenic animal;
- c) measuring the level of B lymphocytes expressing human CD20 in the first transgenic animal;
- d) determining the percent reduction in the level of B lymphocytes between step (a) and step (c);
- e) measuring the level of B lymphocytes expressing human CD20 in a second transgenic animal of claim 1;
- f) administering said agent to the second transgenic animal of claim 1;
- g) measuring the level of B lymphocytes expressing human CD20 in the second transgenic animal; and
- h) determining the percent reduction in the level of B lymphocytes between step (e) and step (g);  
wherein if the percent reduction determined in step (h) is greater than the percent reduction determined in step (d), the agent is identified as capable of inducing an Fc-mediated effector cell response against B lymphocytes expressing human CD20.

21. A method of testing safety of anti- human CD20 therapy, said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in an animal of claims 1 or 9 ;
- b) administering said agent to the animal of claims 1 or 9; and
- c) measuring the level of B lymphocytes expressing human CD20 in the animal;

wherein a decrease in the number of B lymphocytes expressing human CD20 in the animal identifies the agent as capable of depleting or killing cells expressing CD20;

- d) monitoring the animal for short or long term adverse effects.

22. A method of testing efficacy of anti- human CD20 therapy, said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in a set of animals of claims 1 or 9 ;
- b) administering to each animal of the set a different dose of an agent; and
- c) measuring the level of B lymphocytes expressing human CD20 in the animal after each dose;and
- d) determining at least one dose of the agent that results in the most B cell depletion.